REMARKS

The Office Action dated January 24, 2008 presents the examination of claims 47-88. All of these claims are canceled, being replaced by the current claims 89-120. This method of amendment was chosen for its editorial simplicity.

With respect to the amended claims, the new claims 89-99 relate to methods for regulating immune response. Claims 115-119 relate to prophylaxis and treatment of allergic diseases. Both of these groups of claims are consistent with the present examination of Groups I and IV.

Claims 100-114 and 120 relate to adenine compounds of the invention, consistent with the current examination of such claims.

Objection to scope of claims based upon restriction

Claims 77-84 and 88 were "rejected" on the basis that they are directed to an improper Markush group. The Examiner suggests that structural differences among the compounds at "a part of the molecule essential for utility", unity of invention is lacking. The Examiner has required removal of indications that the methods claimed relate to treatment of viral or dermal diseases.

The present claims have been so amended. Applicants reserve the right to file subsequent applications directed to the removed subject matter pursuant to 35 USC § 120.

Rejections over prior art

Claims 47-50, 54, 57, 67-84 and 87-88 are rejected under 35 USC 102(b) as anticipated by U.S. 6329381. The cancellation of the rejected claims renders this rejection moot. Applicants submit that this rejection should not be applied to the present claims.

The prior claims 47-50, 54, 57, 67-84 and 87-88 were directed at a topically administrable composition comprising an adenine compound and methods for using such compounds to regulate an immune response. Claims now reciting the adenine compound per se are represented

by the present claims 100-114 and 120. In these claims, the ring A is recited as being a heteroaromatic ring (claims 100-106), or in instances where ring A is benzene, the ring A is substituted by an alkyl amino substituted ester group (claims 107-114). Neither are the particular compounds of claim 120 mentioned in the '381 patent.

With respect to the method claims 89-99 and 115-119, these claims relate to topical administration for regulating an immune response (e.g. line 2 of claim 89). Nowhere in the reference is there any teaching or suggestion of topical administration of any compound as in the present claims. Such route of administration disclosure as is presented by '381 is at col. 20, lines 34-42, and only oral or parenteral administration, i.e. systemic routes of administration are disclosed.

Accordingly, the instant rejection should not be applied to the present claims.

Claims 47-50, 54, 57, 67-84 and 87-88 are rejected under 35 USC § 103(a) as being unpatentable over U.S. 6329381. The cancellation of the rejected claims renders this rejection moot. Applicants submit that this rejection should not be applied to the present claims.

Before turning to the substance of our argument, Applicants wish to point out that the Examiner's comments at pp. 3 to 5 in support of his obviousness rejection represent an inappropriate stretching of the law of inherency. The Examiner bears the burden of establishing a prima facie case of anticipation or obviousness, and before such is established, the Applicant has no burden of proof or even of argument. The reason that a doctrine of inherency can be asserted at all is that the properties of a compound are considered to be part and parcel of the compound, and to arise from the structure of the compound and its interaction with its environment. An argument that a "similar" compound will have identical properties is inappropriate. An argument that a claim solely recites functional characteristics still requires that the composition of the prior art be the same as that of the claim, as quoted by the Examiner at the top of page 4 of the Office Action.

Nevertheless, in the present application, the invention relates to a genus of compounds, or to particular compounds, as set forth in claims 100-114 and 120, respectively. The compounds are first and foremost defined by structure, and said structure is distinct from what is disclosed as useful in the '381 patent.

Furthermore, the utility ascribed to the compounds in the '381 patent is one of systemic administration to induce interferon activity (col. 2, lines 57-58). On the other hand, as explained above, the present invention relates to compounds useful for topical administration, and that do not produce a systemic interferon response. See, e.g. page 39 at line 16.

Applicants submit that the '381 reference fails to establish *prima facie* obviousness of the claimed invention, as structural aspects of the compound claims are not disclosed or suggested by the reference, and because route of administration elements of the claims are in fact taught away from by the reference.

Furthermore, the compounds and methods of the present invention provide results that are not expected by one of ordinary skill in the art who would read the '381 patent. In particular, as mentioned above, the result that the compounds of the invention have a short half-life in serum, and thus do not provoke any systemic interferon response or indeed do not exhibit significant physiological activity at the systemic level, is unexpected.

The particular advantageous properties of the compounds of the present invention as topical medicaments are especially enjoyed by compounds in which Q^1 or Q^2 is an ester, thioester, or amide (see, e.g. claims 104 and 107-114). In this regard, Applicants provide attached the Declaration of Dr. Yoshiaki Isobe, which compares compounds of the present invention in which Q^1 or Q^2 is an ester with similar compounds in which the ester is absent. In general, a 3- to 10-fold lower effective concentration is seen for the ester compounds in locally inducing an interferon response and in inhibiting local eosinophil infiltration. However, the compounds of

do not produce any systemic rise in interferon levels. Such a result is not expected by one who reads the '381 patent.

For any and all of the above reasons, the instant rejection should not be applied to the present claims.

Rejections for indefiniteness

Claims 47-88 were rejected under 35 USC § 112, second paragraph for a number of particular reasons as set forth at pp 6-7 of the Office Action. Applicants submit that the present claim language is not indefinite and is readily susceptible to interpretation.

1. Q1 is no longer defined twice in the claim.

2. A proper composition claim can in fact recite only a compound, so long as the transitional phrase includes the term "comprising", leaving the claim open to inclusion of a carrier. Notwithstanding this, the present claims are directed to compounds or to methods of use.

3. Dependency of the claims has been corrected.

4. All independent claims include a full definition of formula 1.

5. The recitation of a serum half-life is not at all indefinite. One of ordinary skill in the art knows this means the time by which ½ of the amount of a substance present at time zero is present in the serum. The specification provide at least one method for measuring half-life in serum, and so the claim is readily interpretable.

6. "Liver S9" has been corrected in the specification and in the claims.

7. "Inhalation" is in fact correct and is a mode of topical administration. Applicants submit attached hereto an excerpt from "Pharmaceuticals", revised second edition, Toshiro Murata, editor, and a partial English translation thereof. The Examiner should note the indication on page 7 that "inhalation" is a mode of topical administration to the respiratory tract.

8. Claim 72 is canceled and no similar claim is presented.

Rejection for lack of enablement

Claims 74-77, 79-84 and 87-88 are rejected under 35 USC § 112, first paragraph, for alleged lack of enablement of the claimed subject matter, with respect to demonstration of therapeutic utility. This rejection is respectfully traversed as it might be applied to the now pending claims. Reconsideration and withdrawal thereof are requested.

The Examiner asserts basically that the specification does not provide enough working examples of the invention, and the art is unpredictable.

Example 122 of the present invention provides in vitro results showing that 24 diverse compounds within the scope of the invention induce interferon activity in cultured rat spleen samples. Global antiviral interferon activity is measured in a viral cytotoxicity assay according to a cited reference (Armstrong et al.). Example 123 provides similar data for 49 compounds within the scope of the invention.

The specification clearly describes that interferon production at the local site of application of the compound produces the therapeutic effect of the compound. See, e.g. page 1, line 24 to page 2, line 10 and page 2, lines 17-22. Thus, the specification, taken with what was known in the art at the time the present invention was made, clearly establishes a nexus between the in vitro results provided in the specification and the alleged utility of the invention.

Furthermore, the specification in Example 126 demonstrates efficacy of one compound of the invention in an animal model of asthma well-established in the art. That the compound of the invention is slightly less effective than a present therapy for asthma is of no consequence. For instance, beclamethasome might be considered a positive control.

The Examiner commits reversible error by requiring certainty with respect to pharmaceutical efficacy as a criterion for patentability. Such is not the law. Rather, Applicants' burden is only one of the preponderance of the evidence, meaning that the specification and any post-filing data submitted must only establish that it is more likely than not that the invention will work as asserted.

Furthermore, the *Wands* standard is not that no experimentation is permitted, but that whatever experimentation is needed must not be "undue", meaning that it is not guided and is not expected to have to be performed. Experimentation that one of ordinary skill in the art expects to have to perform to test the limits of the invention, and that is guided by the specification and/or the prior art with respect to how to conduct it, is not undue experimentation, regardless of the amount of testing involved. *See, Ex parte Kubin*, 83 USPQ2d 1410 (BPAI 2007) and *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The present specification discloses a large number of compounds and demonstrates efficacy for the intended utility in vitro and in vivo. Furthermore, the specification expressly describes tests that can be applied by one of ordinary skill in the art to determine if any particular compound is more likely than not to be effective for the asserted utility. Such efficacy testing is very much expected to have to be conducted by one of ordinary skill in the art of drug development.

Accordingly, the full scope of the present claims must be taken to be enabled, and the instant rejection should not be applied to the present claims.

Obviousness-type double patenting

Claims 47-55, 57-61 and 63-88 are provisionally rejected under the judicially-created doctrine of obviousness-type double patenting over claims 1-19 and 21 of co-pending application 10/594,074. The provisional nature of this rejection is noted and Applicants wish to hold this rejection in abeyance until claims are allowed in this application or in the '074 application.

The Examiner's request that Applicants notify the Examiner of any U.S. national filings of WO 2007034917, WO 2007034817 or JP 2005089334 is noted.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a three (3) month extension of time for filing a reply in connection with the present application, and the required fee of $1050.00 is attached hereto.

If the Examiner has any questions concerning this application, the Examiner is requested to contact Mark J. Nuell, Reg. No. 36,623 at the telephone number of (858) 792-8855. Facsimile communications may be sent to the undersigned at the facsimile number of (858) 792-3785.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Dated: July 23, 2008

Respectfully submitted,

By _____
Mark J. Nuell
Registration No.: 36,623
BIRCH, STEWART, KOLASCH & BIRCH, LLP
12770 High Bluff Drive
Suite 260
San Diego, California 92130
(858) 792-8855
Attorney for Applicant